Attorney Docket No. ABI1150-18
(071243-0218)

15/Reopen Recons

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Soon-Shiong and Desai

Title: METHODS AND FORMULATIONS OF TAXANES

Appl. No.: 09/628,387

Filing Date: August 1, 2000

Examiner: A. Pulliam

Art Unit: 1615

CERTIFICATE OF FACSIMILE TRANSMISSION
I hereby certify that this paper is being facsimile transmitted to the United States Patent and Trademark Office, Washington, D.C. on the date below.

*Stephen E. Reiter*
(Printed Name)

Stephen E. Reiter
(Signature)

*September 20, 2002*
(Date of Deposit)

Ret 1-8-03

Commissioner for Patents
Washington, D.C. 20231

## *REPLY UNDER 37 C.F.R. § 1.111*

Sir:

Responsive to the Office Action dated May 20, 2002 ("the Office Action"), please consider the following Remarks.

## *Remarks*

Courtesies extended to Inventor Desai and Applicant's representative during the telephone interview held on August 8, 2002 are acknowledged with appreciation.

### *Description of the Invention*

The present invention provides a quantity of taxane in a vial which corresponds to the dosage for administration, i.e. a unit dosage form of taxane. The unit dosage forms of the present invention allow systemic administration of taxane to a human subject in need thereof at doses and over administration periods and/or treatment cycles not previously possible.

The present invention allows minimal handling of taxane by health care providers, virtually eliminates the need for costly storage and/or disposal of excess product, and reduces

contamination issues for the patient. Minimal handling of taxane is recommended because, as stated in the *Drug Facts and Comparisons* (1994) at page 2785, paclitaxel, for example, is a cytotoxic anticancer drug which could be harmful to those handling the product. For example, gloves are recommended when handling paclitaxel and thorough flushing of the skin or mucous membranes with water is recommended if paclitaxel contacts the skin or mucous membranes. Minimizing the handling of taxane is therefore advantageous and is facilitated by the unit dosage forms of the present invention. For example, the need to obtain drug from multiple separate vials to create the ultimate dosage required by a subject is virtually eliminated because a single unit dosage is provided by the unit dosage form of the present invention. Similarly, the need to dispose of excess product is also eliminated. Disposal of excess product is costly both because taxane itself is very expensive and the actual disposal of excess taxane is by itself costly. Accordingly, the present invention eliminates waste of taxane by providing taxane in a unit dosage form.

***Double Patenting Rejection***

The rejection of claims 1-16, 30-44, 58-78, 98-101, 104-107, 110-113, 116-119, 122-125, 128-131, 133-135, 137-141, 145-147, 149-151, 153-158, 160-162, 164-177 under the judicially created doctrine of double patenting over claims 1-57 of U.S. Patent 6,096,331 is acknowledged. The provisional rejection of claims 1-16, 30-44, 58-78, 98-101, 104-107, 110-113, 116-119, 122-125, 128-131, 133-135, 137-141, 145-147, 149-151, 153-158, 160-162, 164-177 under the judicially created doctrine of double patenting over claims 1-78 of co-pending Application No. 09/628,389 is also acknowledged. These rejections will be addressed after the claims are otherwise in condition for allowance (e.g., by filing a terminal disclaimer or such other action as deemed appropriate).

***Claim Rejections Under 35 U.S.C. §112***

The rejection of claims 1-16, 30-44, 58-78, 98-101, 104-107, 110-113, 116-119, 122-125, 128-131, 133-135, 137-141, 145-147, 149-151, 153-158, 160-162, 164-177 under 35 U.S.C. §

112, first paragraph is respectfully traversed. Applicants respectfully disagree with the Examiner's assertion that elements which are critical or essential to the practice of the invention, but not included in the claims are not enabled by the disclosure. *See* Office Action at page 3.

The invention, as set forth in, for example, claim 1, is drawn to a unit dosage form comprising a sealed vial containing a sufficient quantity of taxane to provide for administration to a subject a total dose of taxane in the range of about 30 mg/m$^2$ to about 1000 mg/m$^2$ over an administration period no greater than about 3 hours. This claim is drawn to an article of manufacture which comprises a sealed vial with a specified amount of taxane in the vial. The specification, along with the level of skill in the art at the time the application was filed, provides adequate enablement for making a vial with a specified amount of taxane in the vial. Therefore, no elements which are critical or essential to the practice of the invention are missing from the claim. Withdrawal of this rejection is therefore respectfully requested.

***Claim Rejections Under 35 U.S.C. §102***

The rejection of claims 1-14, 16, 30-42, 44, 58-76, 78, 98, 99, 101, 104, 105, 107, 110, 111, 113, 116, 117, 119, 122, 123, 125, 128, 129, 131, 133, 135, 137-139, 141, 145, 147, 149, 151, 153-154, 156, 158, 160, 162, 164-168, 170, and 172-177 under 35 U.S.C. 102(b) as allegedly being unpatentable over pages 2780-2785 of the 1994 edition of *Drug Facts and Comparisons*, is respectfully traversed. Applicants' invention as defined, for example, by claim 1, distinguishes over this reference by requiring a unit dosage form comprising a sealed vial containing a sufficient quantity of taxane to provide for administration to a subject a total dose of taxane in the range of about 30 mg/m$^2$ to about 1000 mg/m$^2$ over an administration period no greater than about 3 hours.

Those skilled in the art readily recognize that unit dosage forms comprising taxane in the range contemplated by the present claims were not available as of December 1992. Thus, the dosages mentioned in *Drug Facts and Comparisons* (i.e., 135 mg/m$^2$ to 175 mg/m$^2$) were not

provided in a single vial (i.e., unit dosage form), as required by the present claims. Clearly, only the present invention teaches unit dosage forms comprising taxane in the range of about 30 mg/m$^2$ to about 1000 mg/m$^2$ for administration over three hours.

Applicants respectfully disagree with the Examiner's assertion that *Drug Facts and Comparisons* discloses taxol in single dose vials and that this disclosure anticipates the claims of the present invention. *See* Office Action, pages 5 and 6. The vials mentioned in the reference contain 30 mg paclitaxel/5 ml as single use vials. The claimed dosage ranges mentioned in, for example, claim 1, are about 30 mg/m$^2$ to about 1000 mg/m$^2$. The amount of paclitaxel in these vials is not within the range of the claim. For example, the body surface area of a woman who is 5 feet tall, and weighs 120 lbs is about 1.5 m$^2$. The body surface area of a man who is 5 feet 9 inches tall and who weighs 160 lbs is about 1.9 m$^2$. At a dosage of 30 mg/m$^2$, this is a total dosage of 45 mg taxane for the woman and 57 mg for the man. The vials of the *Drug Facts and Comparisons* teach only 30 mg taxol. Clearly such vials do not cover a single dose even for the lowest claimed dosage range.

Moreover, the Examiner's discussion with regard to total dosages contemplated for administration by *Drug Facts and Comparisons* (i.e., that the FDA approved dosages of paclitaxel are 135 mg/m$^2$ or 175 mg/m$^2$ administered intravenously over three hours every three weeks (*See* Office Action at page 5)) is irrelevant. Because the claimed invention is drawn to unit dosage forms comprising a sealed vial of taxane, the fact that *Drug Facts and Comparisons* teaches a particular total dosage for ultimate delivery to the patient is not pertinent to the claim.

Further, even if these dosages were relevant, the Examiner's assertion that the FDA approved dosages are 135 mg/m$^2$ or 175 mg/m$^2$ administered intravenously over 3 hours every 3 weeks is in error. Specifically, the two doses mentioned by the Examiner are present in *Drug Facts and Comparisons* only in the context of describing the source of the data regarding adverse reactions. Specifically, the reference mentions a randomized trial where two doses were

administered over two dose schedules, i.e., "[t]he eighth study was a randomized trial in patients with ovarian carcinoma comparing two doses (135 or 175 mg/m$^2$) and two dose schedules (3 or 24 hours)." *See* page 2782 of *Drug Facts and Comparisons*. In contrast to the Examiner's assertion, the reference does not recommend these dosages and is silent with respect to whether the dose schedules are effective in patients.

By contrast, *Drug Facts and Comparisons* expressly teaches that a dose of 135 mg/m$^2$ administered over 24 hours is effective, and approved by the FDA. Specifically, at page 2785 the reference states:

> **Administration and Dosage:**
> *Approved* by the FDA on December 29, 1992.
>
> * * *
>
> *Dosage:* A dose of 135 mg/m$^2$ administered IV over 24 hours every 3 weeks is effective in patients with metastatic carcinoma of the ovary after failure of first-line or subsequent chemotherapy.

Thus, even if dosages mentioned in *Drug Facts and Comparisons* were relevant, Applicants respectfully submit that the Examiner has misinterpreted the teachings regarding dosages in the reference.

Applicants respectfully disagree with the Examiner's assertion that claims 1-15, 30-43, 58-77, 98-100, 104-106, 110-112, 116-118, 122-124, 128-130, 133-134, 137-140, 145-146, 149-150, 153-157, 160-161, 164-171 and 177 are allegedly anticipated by page 3558 of *Drug Facts and Comparisions*. *See* Office Action page 6. As discussed above, the fact that this reference recommends particular dosages of docetaxel is irrelevant. What is embraced, for example, by claim 1 is a unit dosage form comprising a sealed vial with a specified quantity of taxane. The reference does not disclose a unit dosage form of a taxane with an amount of taxane within the claimed range. Because *Drug Facts and Comparisons* does not teach the unit dosage forms of

the present invention and does not teach the administration protocol contemplated for use with invention unit dosage forms, the rejection of claims 1-83 under 35 U.S.C. 102(b) is not properly applied. Accordingly, reconsideration and withdrawal are respectfully requested.

***Claim Rejections Under 35 U.S.C. § 103***

The rejection of claims 1-16, 30-44, 58-78, 98-101, 104-107, 110-113, 116-119, 122-125, 128-131, 133-135, 137-141, 145-147, 149-151, 153-158, 160-162, 164-177 under 35 U.S.C. § 103 as allegedly being unpatentable over pages 2780-2785 or page 3558 of *Drug Facts and Comparisons* is respectfully traversed. Applicants' invention, as defined for example by claim 1, distinguishes over *Drug Facts and Comparisons* by requiring a unit dosage form comprising a sealed vial containing a sufficient quantity of taxane to provide for administration to a subject a total dose of taxane in the range of about 30 $mg/m^2$ to about 1000 $mg/m^2$ over an administration period no greater than about 3 hours. In contrast, *Drug Facts and Comparisons* does not teach or suggest unit dosage forms comprising taxane.

In addition, Applicants respectfully submit that the disclosure on either pages 2780-2785 or page 3558 of *Drug Facts and Comparisons* does not fairly suggest the unit dosage forms required by, for example, claim 1. Those skilled in the art would not be motivated to produce a unit dosage form as required by claim 1. One of skill in the art did not have any motivation as of the filing date to prepare a unit dosage form containing a total dose of taxane in the specified range of 30 $mg/m^2$ to about 1000 $mg/m^2$ over an administration period of no greater than 3 hours. As discussed above, *Drug Facts and Comparisons* states that the FDA recommended dose was 135 $mg/m^2$ administered intravenously over 24 hours. Thus, it is respectfully submitted that the rejection under 35 U.S.C. 103(a) is not properly applied. Accordingly, reconsideration and withdrawal of the rejection of claims 1-83 are respectfully requested.

In view of the above remarks, reconsideration and favorable action on all claims are respectfully requested. If any matters remain to be resolved in view of this communication, the

Examiner is invited to contact the undersigned at the telephone number set forth below so that a prompt disposition of this application can be achieved.

Respectfully submitted,

Date: September 20, 2002

Stephen E. Reiter
Registration No. 31,192
Telephone: (858) 847-6711
Facsimile: (858) 792-6773

Foley & Lardner
P.O. Box 80278
San Diego, CA 92138-0278